26. The synthetic conjugate of Claim 23 in which the oligosaccharide comprising α linked galactose is Galα1, 3Gal.

27. The synthetic conjugate of Claim 23 which further comprises a moiety which binds to liver cells.

28. The synthetic conjugate of Claim 27 wherein the moiety which binds to liver cells comprises a β-linked galactose.

REMARKS

The Claims in the case are 23 -28, which are restated versions of Claims 3-10. The issues of multiple dependency have been avoided in the revisions. The claims relate to the elected invention.

The 102 and 103 rejections of the Claims 1-3 have been avoided by the newly added claims. The issues raised by the inclusion of function limitations cited in the rejection of Claims 2-3 under Section 112 are also avoided in the rewritten claims.

The claims in the case are allowable.

The following discussion explains the allowability of the claims in the case over art applied in the prosecution of an equivalent application in the PCT. The references applied against the claims are of record in the prosecution of the parent application, and included in the IDS submitted in the instant application.

It is known that xenogenic natural antibodies are antibodies which are already present in a host or are elicited in the hyperacute rejection of xenografts. The major target of these antibodies appears to be the Galα1, 3Gal which is present on pig tissue but not in humans. The antibodies of the recipient bind to the blood vessels of the donor tissue and activate the complement system of the recipient. The naturally occurring anti- Galα1, 3Gal antibodies in human serum are believed to be a major factor in the hyperacute reaction of discordant organ xenografts. These xenographic natural anti- Galα1, 3Gal can be removed by absorption to a suitable immunoabsorbant, according to reference Xenotransplantation 2, 98-106 (1995), reference AK. In this reference the synthetic

Galα1, 3Gal disaccharide was coupled to glass beads for immunoabsorption. The cytotoxic effect of human serum on pig kidney which expresses Galα1, 3Gal epitopes was almost totally inhibited by adsorption of the serum through immunoaffinity columns. The reference further discloses the injection of soluble synthetic oligosaccharide antigen into the recipient to block the action of the xenogenic natural antibodies. However, conjugates of such oligosaccharides are not described in the reference. In fact the reference covalently links Galα1, 3Galdisaccharides to polyacrylamide. The discussion section of this reference emphasizes the superiority of the conjugates taught when compared to other moieties tested, either when used as soluble substances or when used as insoluble immunoadsorption matrices, see pages 103-105 of this reference. A skilled person following the teaching of this reference and desiring to use Galα1, 3Gal conjugates for the detection, immunoadsorption or inhibition of the cytotoxic activity of anti αGal antibodies would use the specific PAA- Galα1, 3Gal conjugates disclosed in the article.

There is no teaching or indication in the references that would lead a skilled person toward a synthetic conjugate described in the present application that comprises a protein linked to a plurality of epitopes. This reference does not even mention conjugates of the type used in the present invention. It is pointed out that the structure of polyacrylamide is very different from that of proteins. It is therefore quite unpredictable that the results obtained for PAA- Galα1, 3Gal conjugates would apply to protein- Galα1, 3Gal conjugates. On the contrary and as explained above, the reference emphasizes the importance of using specific PAA- Galα1, 3Gal conjugates.

The reference AC, J. Exp. Med. 166, 419-432 (1987), discloses that laminin, a natural glycoprotein with a terminal Galα1, 3Gal group is able to bind to serum anti-antibodies responsible for binding to blood vessels, or striated muscle and the like. This application teaches and claims synthetic protein conjugates. It was published nine years before the filing of the present application. It emphasizes that circulating antibodies to mouse laminin in Chagas disease, American cutaneous leishmaniasis and also present in normal individuals recognize terminal galactosyl α1, 3- galactose epitopes. This reference addresses the specific technical problem of identifying particular epitopes involved in parasitic diseases. Mouse laminin was a convenient tool for identifying such epitopes since mice are convenient test animals and since it was known that laminin was able to bind most tissue-reacting antibodies present in sera from patients infected with Trypanosomatidae. There is no indication that mouse laminin could be used in any treatment. In any event, mouse laminin is a